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THE BIOLOGY OF DEATH—IV. THE CAUSES OF DEATH[1]

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I. CLASSIFICATION OF THE CAUSES OF DEATH

WE have seen in earlier papers that natural death of the metazoan body comes about fundamentally because of the differentiation of structure and function in that body. It is a complex aggregate of cells and tissues, all mutually dependent upon each other and in a delicate state of adjustment and balance. If one organ for any accidental reason, whether internal or external, fails to function normally it upsets this delicate balance, and if normal functioning of the part is not restored, death of the whole organism eventually results. Furthermore, we have been impressed by the fact that death does not strike in a haphazard or random manner, but instead in a most orderly way. There are certain periods of life—notably youth—where only an insignificant fraction of those exposed to risk ever die. At other ages, as, for example, extreme old age and early infancy, death strikes with appalling precision and frequency. Further we recall with Seneca that *nascimus uno modo multis morimur.* Truly there are many ways of dying. The fact is obvious enough. But what is the biological meaning of this multiplicity of pathways to the River Styx? There is but one pathway into the world. Why so many to go out? To the consideration of some phases of this problem I invite attention in this paper.

By international agreement among statisticians the causes of human mortality are, for statistical purposes, rather rigidly defined and separated into something over 180 distinct units. It should be clearly understood that this convention is distinctly and essentially statistical in its nature. In recording the statistics of death the registrar is confronted with the absolute necessity of putting every death record into some category or other in respect of its causation. However complex biologically may have been the train of events leading up to a particular demise, the statistician must record the terminal "cause of death" as some particular thing. The International Classification of the Causes of Death is a code which is the result of many years' experience and thought. Great as are its defects in certain particulars, it nevertheless has certain marked advantages, the most conspicuous of which is that by its use the vital statistics of different countries of the world are put upon a uniform basis.

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[1] Papers from the Department of Biometry and Vital Statistics, School of Hygiene and Public Health, Johns Hopkins University, No. 31.

The several separate causes of death are grouped in the International Classification into fourteen general classes. These are:

I. General diseases.
II. Diseases of the nervous system and of the organs of special sense.
III. Diseases of the circulatory system.
IV. Diseases of the respiratory system.
V. Diseases of the digestive system.
VI. Non-venereal diseases of the genito-urinary system and annexa.
VII. The puerperal state.
VIII. Diseases of the skin and of the cellular tissue.
IX. Diseases of the bones and organs of locomotion.
X. Malformation.
XI. Early infancy.
XII. Old age.
XIII. External causes.
XIV. Ill-defined diseases.

Perhaps the most outstanding feature which strikes one about the International List is that it is not primarily a biological classification. Its first group, for example, called "General Diseases," which caused in 1916 in the Registration Area of the United States approximately one-fourth of all the deaths, is a most curious biological and clinical mélange. It includes such diverse entities as measles and malaria, tetanus and tuberculosis, cancer and gonococcus infection, alcoholism and goiter, and many other unlike causes of death. For the purposes of the statistical registrar it perhaps has useful points to make this "General diseases" grouping, but it clearly corresponds to nothing natural in the biological world. Again in such parts of the scheme as do have some biological foundation the basis is different in different rubrics. Some have an organological basis, while others have a causational.

For purposes of biological analysis I developed some time ago an entirely different classification of the causes of death, on what I think is a reasonably consistent basis. The underlying idea of this new classification was to group all causes of death under the heads of the several organ systems of the body, the functional breakdown of which is the immediate or predominant cause of the cessation of life. All except a few of the statistically recognized causes of death in the International Classification can be assigned places in such a biologically grouped list. It has a sound logical foundation in the fact that, biologically considered, death results because some organ system, or group of organ systems, fails to continue its functions.

The headings finally decided upon in the new classification were as follows:

I. Circulatory system, blood and blood-forming organs.
II. Respiratory system.
III. Primary and secondary sex organs.
IV. Kidneys and related excretory organs.
V. Skeletal and muscular systems.
VI. Alimentary tract and associate organs concerned in metabolism.
VII. Nervous system and sense organs.
VIII. Skin.
IX. Endocrinal system.
X. All other causes of death.

The underlying idea of this rearrangement of the causes of death is to put all those lethal entities together which bring about death because of the functional organic breakdown of the same general organ system. The cause of this functional breakdown may be anything whatever in the range of pathology. It may be due to bacterial infection; it may be due to trophic disturbances; it may be due to mechanical disturbances which prevent the continuation of normal function; or to any other cause whatsoever. In other words; the basis of the classification is *not* that of pathological causation, but it is rather that of organological breakdown. We are now looking at the question of death from the standpoint of the pure biologist, who concerns himself not with what causes a cessation of function, but rather with what part of the organism ceases to function, and therefore causes death.

In a series of papers already published I have given a detailed account of this classification, and the reasoning on which particular causes of death are placed in it where they are. Space is lacking here to go into the details, and I must consequently ask the reader either to take it on faith for the time being that the classification is at least a fairly reasonable one, or to take the trouble to go over it in detail in the original publication.[2]

2. General Results of Biologically Classified Death Rates

Here I should like to present first some general statistical results of this new classification. The data which we shall first discuss were in the form of death rates per hundred thousand living at all ages from various causes of death, arranged by organ systems primarily concerned in death from specified diseases. The statistics came from three widely separated localities and times, viz., (a) from the Registration Area of the United States; (b) from England and Wales; and (c) from the City of Sao Paulo, Brazil.

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[2] Cf. particularly Pearl, R. "On the embryological basis of human mortality." (Proc. Natl. Acad. Sci. Vol. 5, pp 593-598, 1919) and "Certain evolutionary aspects of human mortality rates." (Amer. Natl. Vol. LIV. pp. 5-44, 1920). The following section as well as section 4 of this paper are largely based upon the second of the two papers.

The summarized results are shown in graphic form in Fig. 1.

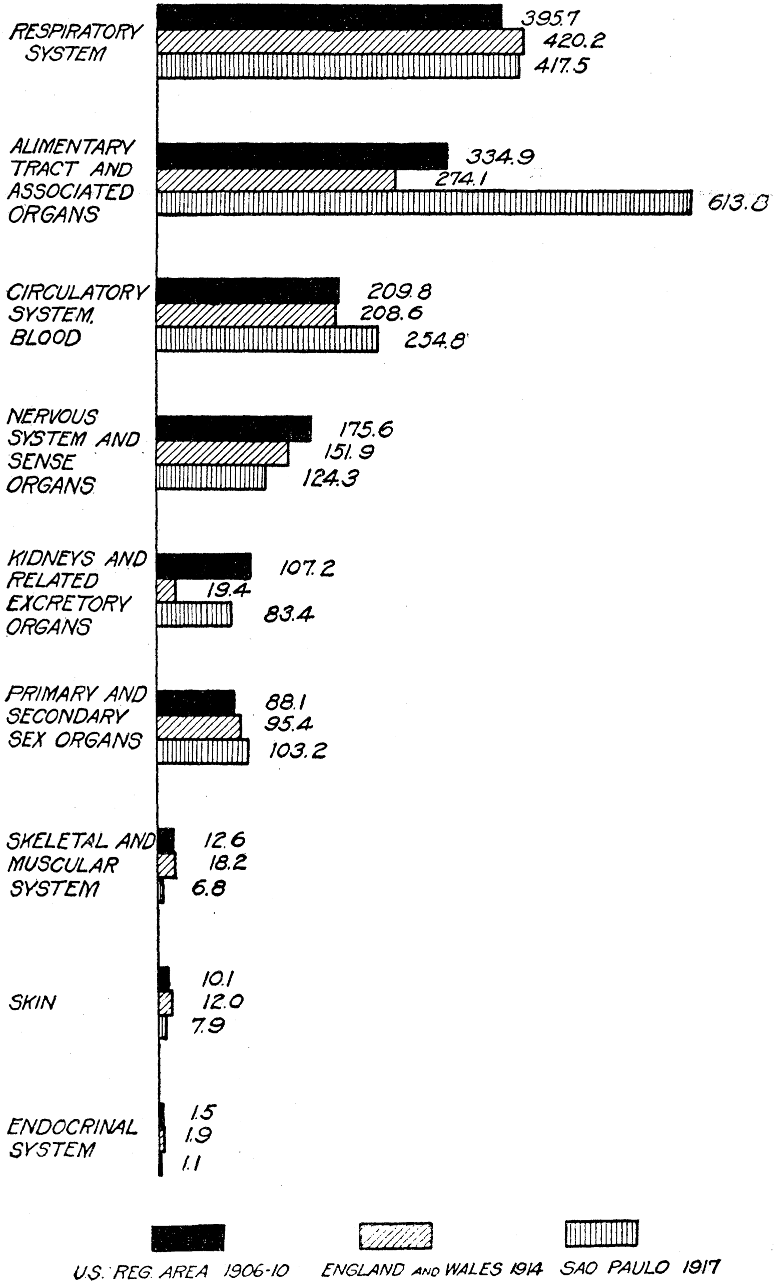

FIG. 1. SHOWING THE RELATIVE IMPORTANCE OF THE DIFFERENT ORGAN SYSTEMS IN HUMAN MORTALITY

In the United States, during the decade covered, more deaths resulted from the breakdown of the respiratory system than from the failure of any other organ system of the body. The same thing is true of England and Wales. In Sao Paulo the alimentary tract takes first position, with the respiratory system a rather close second. The tremendous death rate in Sao Paulo chargeable to the alimentary tract is chiefly due to the relatively enormous number of deaths of infants under two from diarrhea and enteritis. Nothing approaching such a rate for this catagory as Sao Paulo shows is known in this country or England.

In all three localities studied the respiratory and the alimentary tract together account for rather more than half of all the deaths biologically classifiable. These are the two organ systems which, while physically internal, come in contact directly at their surfaces with environmental entities (water, food, air) with all their bacterial contamination. The only other organ system directly exposed to the environment is the skin. The alimentary canal and the lungs are, of course, in effect invaginated *surfaces* of the body. The mucous membranes which line them are far less resistant to environmental stresses, both physical and chemical, than is the skin with its protecting layers of stratified and cornified epithelium.

The organs concerned with the blood and its circulation—the heart, arteries and veins, etc.—stand third in importance in the mortality list. Biologically the blood, through its immunological mechanism, constitutes the second line of defense which the body has against noxious invaders. The first line is the resistance of the outer cells of the skin and the lining epithelium of alimentary tract, lungs, and sexual and excretory organs. When invading organisms pass or break down these first two lines of defense the battle is then with the home guard, the cells of the organ system itself, which, like the industrial workers of a commonwealth keep the body going as a whole functioning mechanism. Naturally it would be expected that the casualties would be far heavier in the first two defense lines (respiratory and alimentary systems and the blood and circulation) than in the home guard. Death rates when biologically classified bear out this expectation.

It is at first thought somewhat surprising that the breakdown of the nervous system is responsible for more deaths than that of the excretory system. When one bears in mind however the relative complexity of the two pieces of machinery it is perceived that the relative position of the two in responsibility for mortality is what might reasonably be expected.

In the United States the kidneys and related excretory organs are responsible for more deaths than the sex organs. This relation is reversed in England and Wales and in Sao Paulo. This difference is mainly due in the case of England to two factors premature birth and cancer. In Sao Paulo it is due to premature birth and syphilis. The higher premature birth rate for these two localities as compared with the United States might conceivably be explained in either of two ways. It might mean better obstetrics here than in the other localities, or it might mean that the women of this country as a class are somewhat superior physiologically in the matter of reproduction, when they do reproduce. The first suggestion seems definitely more improbable than the second. The higher apparent syphilis rate of Sao Paulo probably means nothing more than better reporting, a less prudish disinclination to report syphilis as a cause of death in Sao Paulo than in the other two countries. It is by no means beyond the bounds of possibility that if all deaths really due to syphilis and gonorrhea were actually reported as such, the rate for the sex organs would be decidedly higher than for the excretory organs in all countries.

The last three organ systems, skeletal and muscular system, skin and endocrinal organs, are responsible for so few deaths relatively as not to be of serious moment.

There is one general consequence of these results upon which I should like to dwell a moment longer. In a broad sense the efforts of public health and hygiene have been directed against the affections comprised in the first two items in the chart, those of the respiratory system and the alimentary tract. The figures for the two five-year periods in the United States, 1901-05 and 1906-10, indicate roughly the rate of progress such measures are making, looking at the matter from a broad biological standpoint. In reference to the respiratory system there was a decline of fourteen per cent in the death rate between the two periods. This is substantial. It is practically all accounted for in phthisis, lobar pneumonia and bronchitis. For the alimentary tract the case was not so good—indeed far worse.

Between the two periods the death rate from this cause group fell only 1.8 per cent. All the gain made in typhoid fever was a great deal more than offset by diarrhea and enteritis (under two), congenital debility and cancer. Child welfare, both prenatal and postnatal, seems by long odds the most hopeful direction in which public health activities can expect at the present time substantially to reduce the general death rate. This is a matter fundamentally of education. Ignorant and stupid people must be taught, gently if possible, forcibly if necessary, how to take care of a baby, both before and after it is born. It seems at present unlikely, that mundane law will regard feeding cucumber to a two months' old baby, or dispensing milk reeking with deadly poison makers, as activities accessory to first-degree murder.

But we are moving in that direction under the enthusiastic and capable leadership of the Federal Children's Bureau. And there is this further comfort, that if that final Judgment Seat, before which so many believe we must all eventually appear, dispenses the even-handed justice which in decncy it must, many of our most prominent citizens who in the financial interests of themselves or their class block every move towards better sewage disposal, water and milk supply, and the like, or force pregnant women to slave over a washtub and sewing bench that they may live, will find themselves irrevocably indicted for the wanton and willful slaughter of innocent babies.

3. Specific Death Rates Biologically Classified

Up to this point in our discussions we have been dealing with crude death rates uncorrected for the age and sex distributions of the populations concerned. It is, of course, a well known fact that differences in age and sex constitution of populations may make considerable differences in crude death rates in cases where no real differences in the true force of mortality exist. What is essential for the further prosecution of the analysis of the causes of death is to get *specific* death rates for the several causes. By an age and sex specific death rate is meant the rate got by dividing the number of persons of a *particular specified age and sex* dying from a particular cause by the total number of persons living in the same population *of the same age and sex.* In other words we need to get as the divisor of our rate fraction the number of persons who can be regarded as truly exposed to risk. This exposed-to-risk portion of the population is never correctly stated in a crude death rate. For example, a person now 75 years old can not be regarded as exposed to risk of death at age 45. He was once exposed to that risk but passed it safely. Yet in a crude death rate he is counted with those of age 45.

With the aid of Dr. William H. Davis, director of vital statistics in the Census Bureau, who very kindly provided me with the necessary unpublished data, it has been possible to calculate the specific death rates for each of the 189 causes of death of the International List, for each sex separately, and for each age in 5 year groups, for the United States Registration Area exclusive of North Carolina, in 1910. These results have been put together in the biological scheme of classification and may be presented briefly in the form of diagrams.

Let us first consider deaths from all causes taken together, in order to refresh our memories as to the general form of a death rate curve. It will be noted at once that the rates are plotted along the vertical axis on what strikes one at first as a peculiar scale. The scale is logarithmic. The horizontal lines are spaced in proportion to the logarithms of the numbers at their left, instead of in proportion to the numbers themselves. The advantages of this method of plotting in the present case are two-fold. First, it is possible to get a much wider range of values on the diagram; and second the logarithmic scale permits direct and accurate estimation of the rate of change of a variable. A straight line forming an angle with the horizontal on a logarithmic scale means that the variable is increasing or decreasing, as the case may be, *at a constant rate of change.*

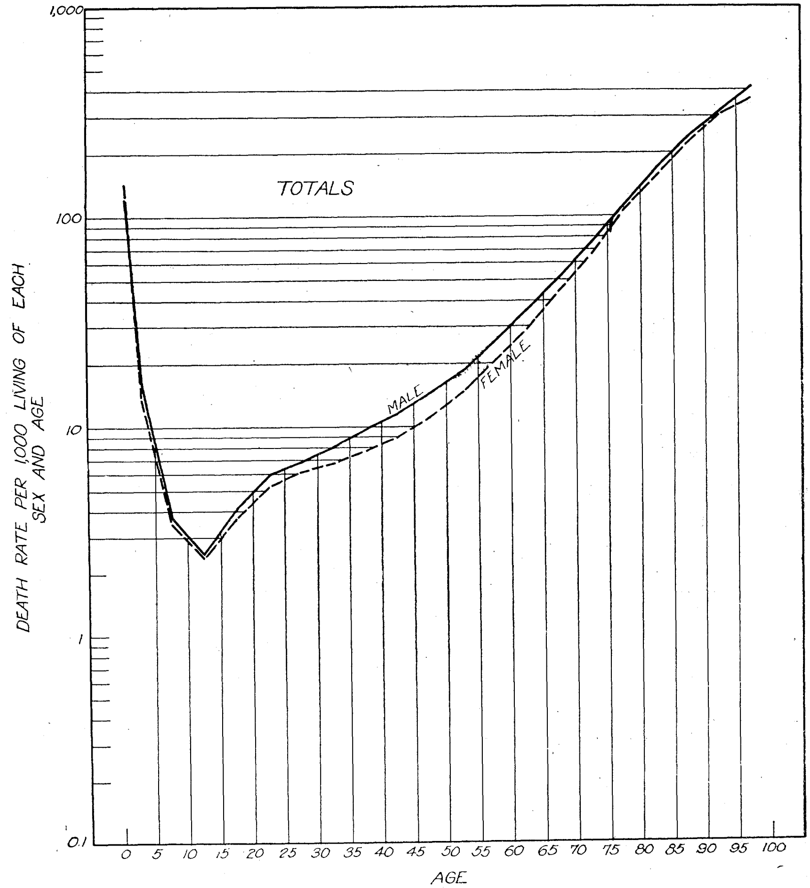

FIG. 2. DIAGRAM SHOWING THE SPECIFIC DEATH RATE AT EACH AGE FOR DEATHS FROM ALL CAUSES TAKEN TOGETHER

Fig. 2 gives the specific death rates for the combined total of all causes. The curve in general has the form of a V with one limb much extended and pulled over to the right. Examining it more in detail, we note that in the first year of life the specific death rate, or, as we may roughly call it, the force of mortality, bears heavier on female infants than on the males. Out of a thousand exposed to risk, 124 male babies die in that year, and 143 female. This is the only year of life in which the total force of mortality is heavier among females than males. From that time on to the end of the span of life the female curve lies, by greater or less amounts, below the male curve. After the heavy mortality of early infancy, the curve drops in almost a straight line to the age period 10-15, where it reaches its lowest point, and only approximately 2½ persons out of a thousand exposed to risk die. The specific mortality curve then begins to rise and continues to do so at an approximately constant and rapid rate for ten years—that is to the age period 20-25. From then on to the age period 50-55 it rises at a slower but constant rate. This is the period of middle life, and here the female curve drops farther below the male curve than at any other place in the span of life. After the age period 50-55 with the on-coming of old age, both male and female curves begin again to rise more rapidly. They continue this rise at a practically constant rate of increase to the end of life, which is here taken as falling in the age period 95-100. In

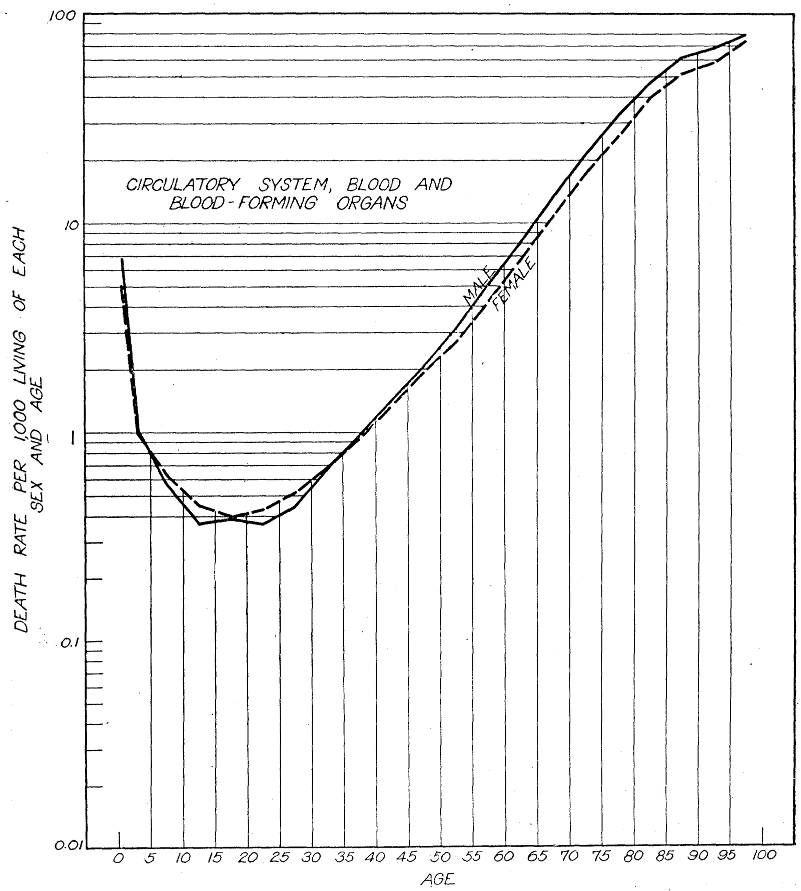

FIG. 3. DIAGRAM SHOWING THE SPECIFIC DEATH RATE AT EACH AGE FROM BREAKDOWN OF THE CIRCULATORY SYSTEM, BLOOD AND BLOOD FORMING ORGANS

this last class the rate has become very high. Out of 1,000 persons living at the ages of 95 and 100, and therefore exposed to risk of death within that period, 494 males and 473 females die, taking an average for the whole five-year period. Of course, before the completion of the period, practically all of the thousand will have passed away.

The important things to note about this curve are these: First, the highest specific forces of mortality occur at the extreme ends of life, and are higher at the final end than at the beginning. In the second place, there is a sharp and steady drop in almost a straight line from the high specific force of mortality in infancy to the low point at about the time of puberty. From then on to the end of the span of life the force of mortality becomes greater every year at a nearly constant rate of increase with only such slight deviations from this constancy of rate as have already been pointed out.

Turning next to the mortality of our first biological group—namely, deaths caused by breakdown of the circulatory system, blood and blood forming organs—we note a marked difference in the form of the curve from what we have seen for the case of all causes of death. In the first place, the specific force of mortality of this group of causes is relatively low in infancy and childhood. Out of a thousand infants of each sex exposed to risk, only 7 males and 5 females die from breakdown of this group of organs during the first year of life. The trough of the curve associated with the mortality of childhood and youth is very much less pointed than in the case of "all causes." It is a smoothly rounded, rather than a sharply pointed depression. It is also noteworthy that between approximately the ages of 5 and 35 the specific force of mortality from diseases of the circulatory system and related organs is higher for females than it is for males. This condition of affairs is probably connected with the graver physiological changes and readjustments called forth by puberty in the female than accompany the same vital crisis in the male. From early adult life, say age 25-30 on, the specific death rate from diseases of the circulatory system and related organs increases at an almost absolutely constant rate until age 85 is reached. After that the rate of increase slows down somewhat. Of those reaching the age 95-100, between 70 and 80 out of each thousand living die from breakdown of this group of organs.

The specific mortality curve for deaths from breakdown of the respiratory system, as shown in Fig. 4, presents a number of points of peculiar interest. In the first place we note that this organ system is much more liable to breakdown than is the circulatory system during all the earlier years of life up to about age 60-65. The decline in the curve from the high point of infancy to the low point of the period about puberty is more sharp and sudden than that of the circulatory system curve. Again, however, just as in the former case, we note that the specific force of mortality from breakdown of this organ system impinges more heavily upon females than upon males in the years from 5-20. This difference is probably connected, as before, with the greater physiological disturbance of puberty in the female than in the male. The lowest point of the respiratory curve falls in the age group 10-15. Between the ages 25-70 there is a very striking difference in the two sexes in respect of specific mortality from breakdown of the respiratory system. The male curve rises in nearly a straight line, while the female curve lies far below it, and actually shows a point of inflection at about age 45 becoming for a short period convex to the base. The explanation for the great separation of the two curves in this period is probably fundamentally occupational. From the nature of their activity males during this period of life are probably subject to a greater risk of breakdown of the respiratory system than are the more protected female lives. From age 70 on, both curves ascend with

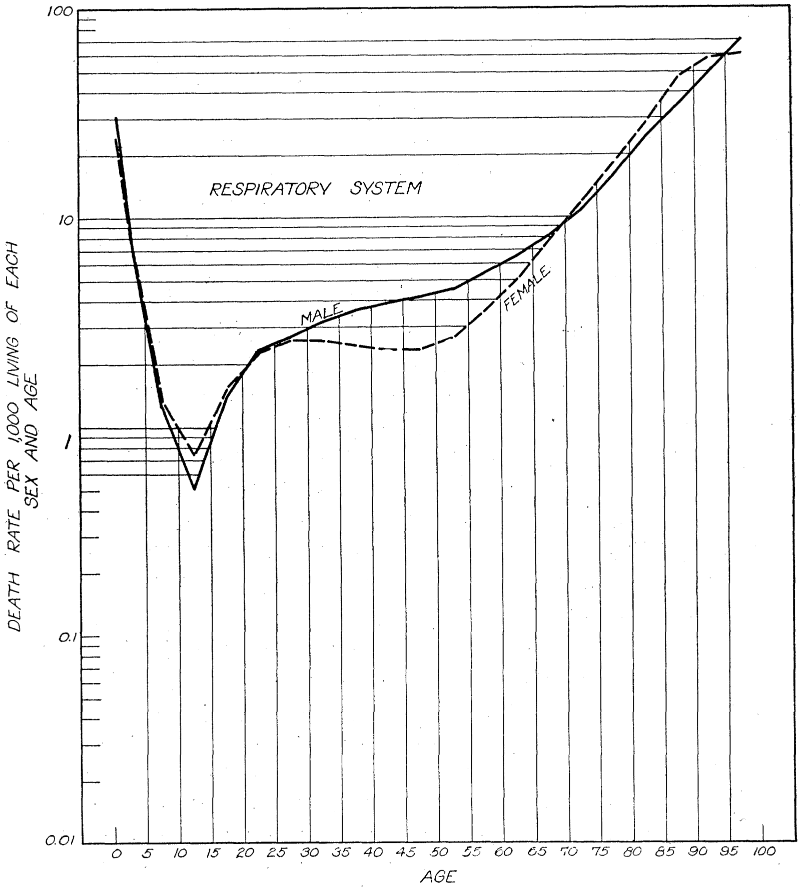

FIG. 4. DIAGRAM SHOWING THE SPECIFIC DEATH RATE AT EACH AGE FROM BREAKDOWN OF THE RESPIRATORY SYSTEM

increased rapidity, the female curve rising above the male, presumably in compensation for the marked dip which it exhibits in middle life. It is, of course, well known that respiratory mortality bears heavily upon the aged.

The next group which we shall consider has to do with deaths from breakdown of the primary and secondary sex organs. This cause group furnishes an extremely interesting pair of curves shown in Fig. 5. Before discussing in detail their form a word of explanation as to their makeup should be given. In this rubric are included "Premature birth" and "Injuries at birth." The question at once arises, why should these two items, "Premature birth" and "Injuries at birth" be included with the primary and secondary sex organs, since it is obvious enough that the infants whose deaths are recorded under these heads in the vast majority of cases, if not all, have nothing whatever the matter with either their primary or secondary organs. The answer is, in general terms, that on any proper biological basis, deaths coming under of these two categories are not properly chargeable organically against the infant at all, but should be charged, on such a basis, against the mother. To go further into detail, it is apparent that when a premature birth occurs it is because the reproductive system of the mother, for some reason or other, did not rise to the demands of the situation of carrying the foetus to term. Premature birth, in short, results from a failure or breakdown in some particular of the *maternal reproductive system.* This failure may be caused in various ways, which do not here concern us. The essential feature from our present viewpoint is that the reproductive system of the mother does breakdown, and by so doing causes the death of the infant, and that death is recorded statistically under this title "Premature birth." The death organically is chargeable to the mother.

A considerable number of cases of premature birth are unquestionably due to placental defects and the placenta is a structure of foetal origin, so such deaths could not be properly charged to the mother. On the other hand, however, they would still stay in the same table because the placenta may fairly be regarded as an organ intimately concerned in reproduction.

The same reasoning which applies to premature births, *mutatis mutandis,* applies to the item "Injuries at birth." An infant death recorded under this head means that some part of the reproductive mechanism of the mother, either structural or functional, failed of normal performance in the time of stress. Usually "injury at birth" means a contracted or malformed pelvis of the mother. But in any case the death is purely external and accidental from the standpoint of the infant. It is organically chargeable to a defect of the sex organs of the mother. The female pelvis, in respect of its conformation, is a secondary sex character.

Turning now to the consideration of Fig. 5, which gives the curves of specific mortality from breakdown of the reproductive organs we note at once the high specific death rate of infants under one recorded by the female line. This rate is over 40 per thousand exposed to risk. It includes of course both male and female infants dying from congenital debility, premature birth and injuries at birth, because according to the reasoning just explained these deaths are organically chargeable to breakdown or failure to function properly of the reproductive organs of the mother. These deaths, therefore, go into the female group. By the fifth year of life the specific rates of mortality chargeable to reproductive organs have dropped in both sexes practically to zero, amounting to less than 0.01 per thousand exposed to risk. At about the time of puberty the female curve begins to rise and goes up very steeply. By age 30 it has reached a value of 1 per thousand ex-

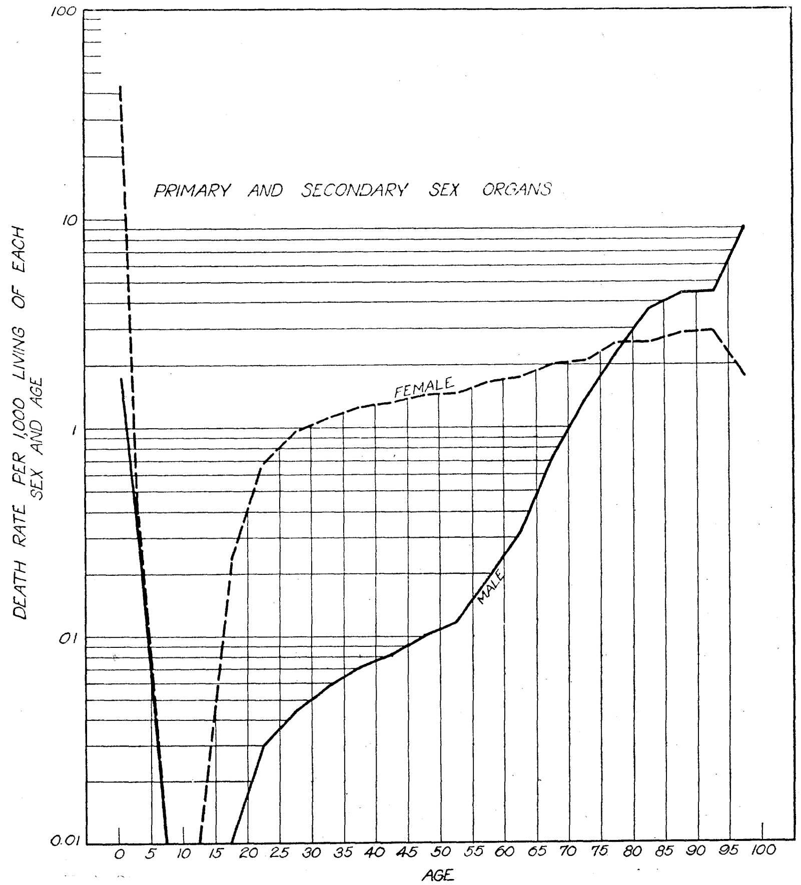

FIG. 5. DIAGRAM SHOWING SPECIFIC DEATH RATES AT EACH AGE FROM BREAKDOWN OF THE PRIMARY AND SECONDARY SEX ORGANS

posed to risk. From that point the force of this specific mortality rises slowly, but at a practically constant rate, to extreme old age. The male curve is in striking contrast to the female. From about age 20 it rises steadily, at an almost constant rate of increase, but a much slower one than the female, until the end of the life span. It crosses the female curve—indicating a higher specific rate of mortality from breakdown of the reproductive organs in men than in women—for the first time at about age 78. This is of course, the time of life when disturbed functioning of the prostate gland in the male begins to take a relatively heavy toll.

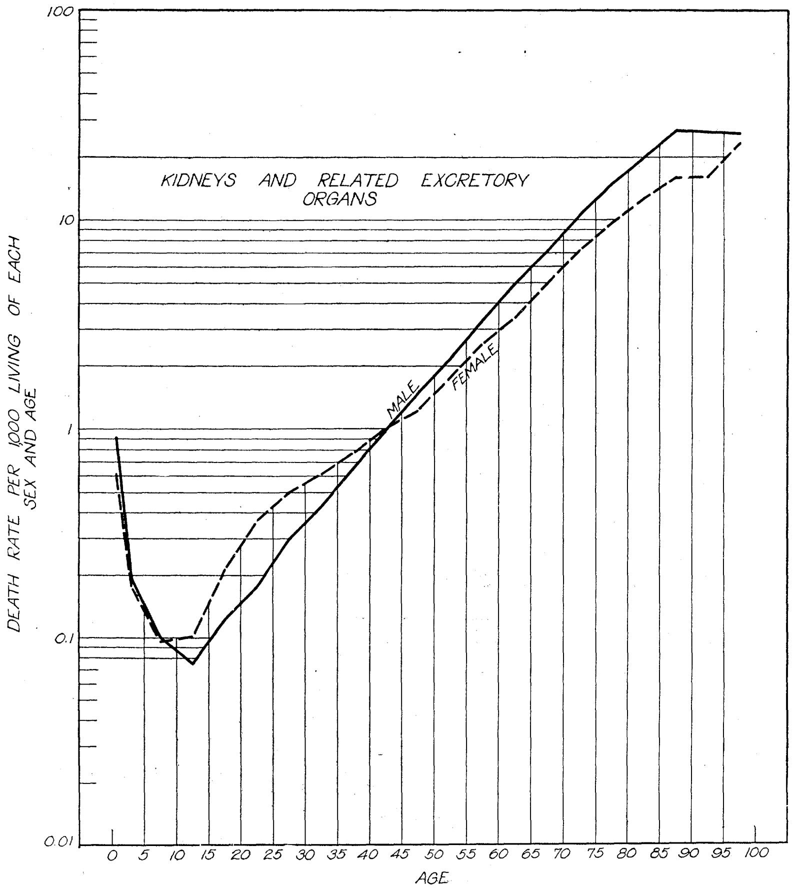

FIG. 6. DIAGRAM SHOWING SPECIFIC DEATH RATES AT EACH AGE FROM BREAKDOWN OF THE KIDNEYS AND RELATED EXCRETORY ORGANS

Fig. 6 shows specific rates of mortality from breakdown of the kidneys and related excretory organs. Death from these causes is relatively infrequent in infancy and early childhood. The low point

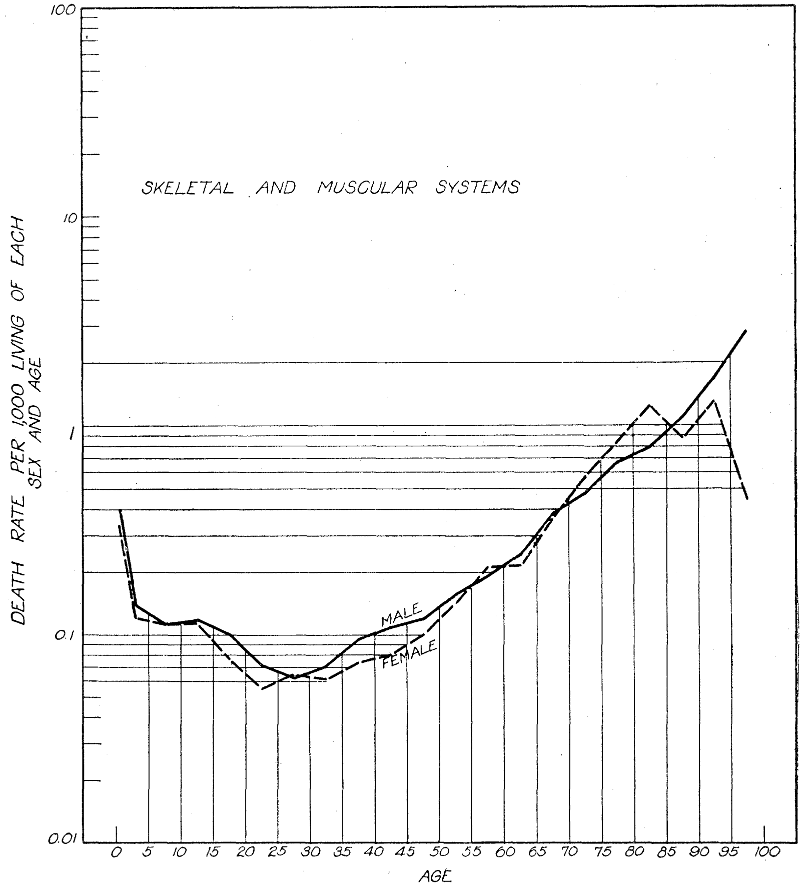

FIG. 7. DIAGRAM SHOWING SPECIFIC DEATH RATES AT EACH AGE FROM BREAKDOWN OF THE SKELETAL AND MUSCULAR SYSTEMS

is reached, as in so many of the other cases, at about the time of puberty. From then on practically to the end of the span of life the specific force of mortality from excretory failure increases at an almost constant rate. During the reproductive period from about 15 to 45 years of age specific rates of mortality from these causes are higher in the female than in the male. After that point the male curve is higher. The relatively heavy specific mortality of the female in early life is undoubtedly due to the heavy strain put upon her excretory organs by child-bearing.

The specific force of mortality from breakdown of the skeletal and muscular systems shown in Fig. 7 presents an interesting pair of curves. Throughout the span of life there is practically no difference between the female and male in the incidence of this mortality, the curves winding in and out about each other. The striking characteristics of the

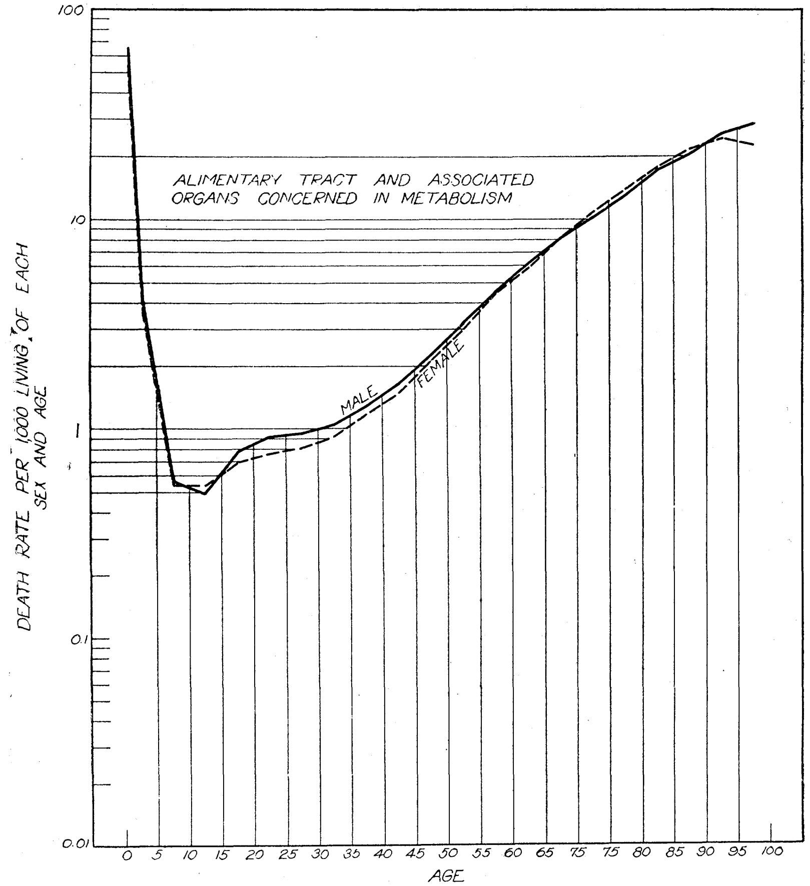

FIG. 8. DIAGRAM SHOWING THE SPECIFIC RATES OF DEATH AT EACH AGE FROM BREAKDOWN OF THE ALIMENTARY TRACT AND ASSOCIATED ORGANS OF METABOLISM

curve are: first, that the specific forces of mortality are absolutely low for these organ systems; and second, that the minimum point is reached not as in most of the other cases around the time of puberty, but at a much later period—namely in the late twenties. The whole curve shows a very gradual change in the rates.

The next diagram, Fig. 8, shows one of the most significant organ groups in the force of its specific mortality. Breakdown and failure to function properly of the primary organs of metabolism—the organs which transform the fuel of the human machine into vital energy—occur with relatively heavy frequency at all periods of life. These curves are among the few which show an absolutely higher specific force of mortality in infancy than in extreme old age. There is practically no significant difference between the male and female curve at any portion of life. During early adult life the female curve lies be-

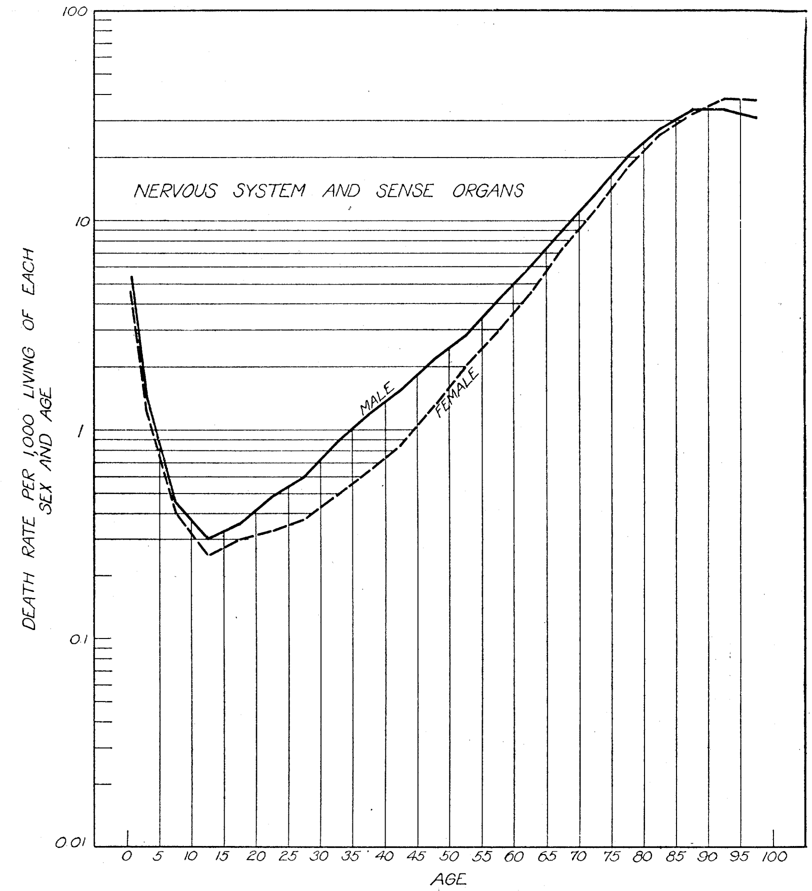

FIG. 9. DIAGRAM SHOWING THE SPECIFIC DEATH RATES AT EACH AGE FROM BREAKDOWN OF THE NERVOUS SYSTEM AND SENSE ORGANS

low the male, but by only a small amount. Out of every thousand infants under one, about sixty die in the first year of life from breakdown of the alimentary tract and its associated organs. After the low point, which falls in the relatively early period of 7 to 12 years of age, there is a rapid rise for about ten years in the specific rates of mortality, followed by a slowing off in the rate of increase for the next ten or fifteen years, after which point the curve ascends at a practically uniform rate until the end of the span of life.

Fig. 9 shows the trend of the specific mortality from breakdown of the nervous system and sense organs. This organ group on the whole functions very well, giving a relatively low rate of mortality until towards the end of middle life. Then the specific rates get fairly large. The low point in this curve is, as in most of the others, at about the time of puberty. From then on to the end of the life span

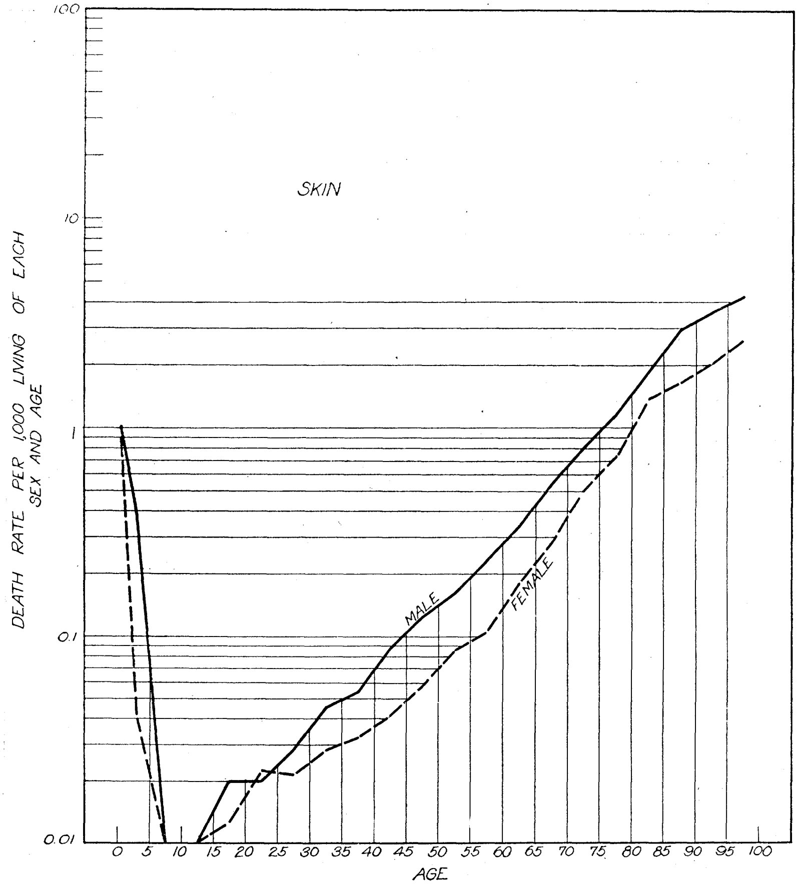

FIG. 10. DIAGRAM SHOWING THE SPECIFIC DEATH RATES AT EACH AGE CHARGEABLE AGAINST THE SKIN

the specific rates increase at a practically uniform rate. The female curve everywhere lies below the male curve except at the extreme upper end of the life span. Before that time, and particularly between the ages of 20 and 50, the business of living evidently either imposes no such heavy demand on the nervous system of the female as it does on that of the male, or else the nervous system of the female is organically sounder than that of the male. The former suggestion seems the more probable.

That breakdown and failure to function properly of the skin as an organ system is a relatively insignificant factor in human mortality is demonstrated by Fig. 10. From a specific death rate of about 1 per 1,000 in the first year of life it drops abruptly practically to zero in early childhood. At about the time of puberty it begins to rise again and ascends at a steady rate during all the remainder of life. The final high point reached is absolutely low, however, amounting to a specific death rate among those exposed to risk of only a little more than 4 per 1,000 at the extreme end of life. The female curve lies well below the male curve practically throughout its course.

Deaths from failure to function properly of the organs of the endocrinal system, including the thyroid gland, suprarenal glands, etc., do not become significant until middle life in the case of the male, as shown in Fig. 11, although in the female the curve begins to rise from puberty on. The specific rates at all ages, of course, are extremely small, practically never rising to more than 1/10 of one person per 1,000 exposed to risk. The well-known fact that these glandular organs, whose secretions are so important for the normal conditions of life, are much more unstable and liable to breakdown in the female than in the male is strikingly shown by this diagram.

Finally, we have the diagram for our *omnium gatherum* group, the "All other causes of death," in Fig. 12. Here we see that because of

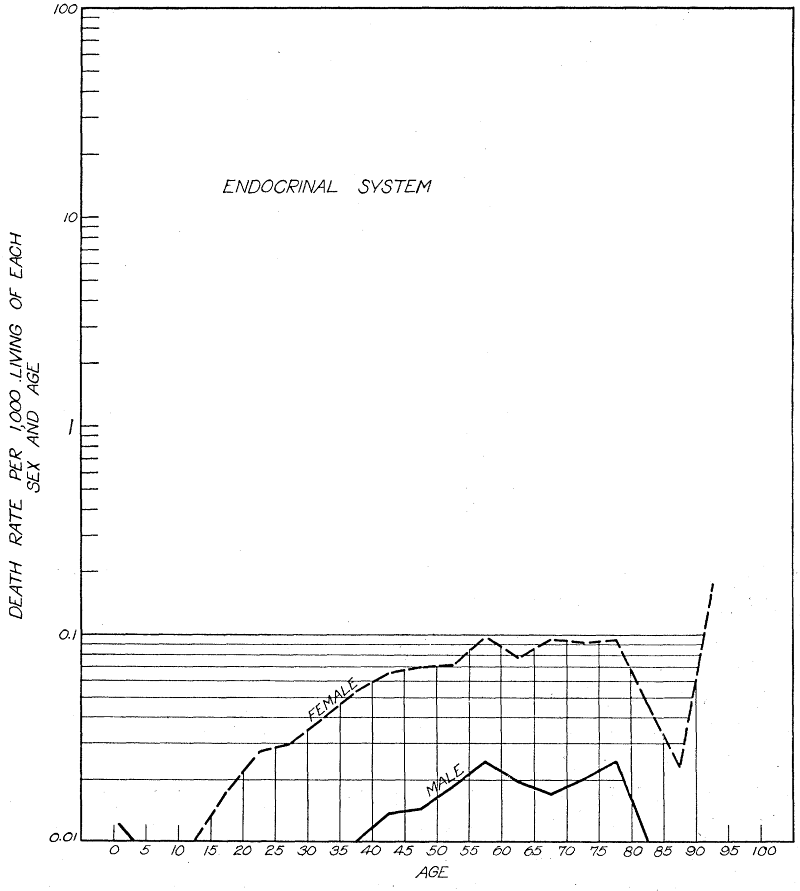

FIG. 11. DIAGRAM SHOWING THE SPECIFIC DEATH RATES AT EACH AGE FROM BREAKDOWN OF THE ENDOCRINAL SYSTEM

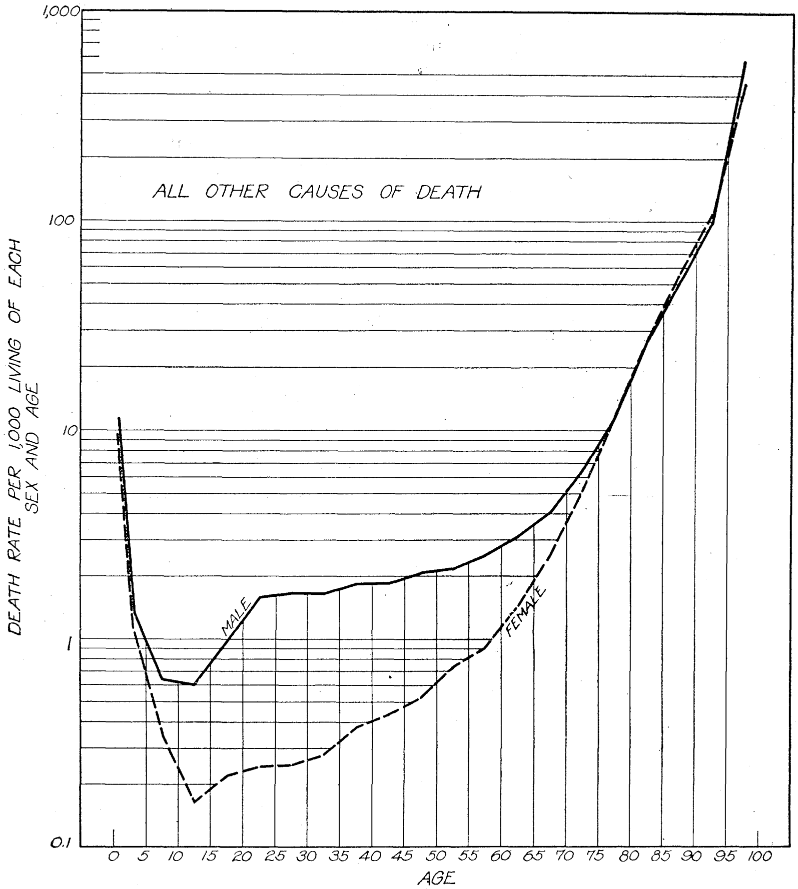

FIG. 12. DIAGRAM SHOWING THE SPECIFIC DEATHS FROM ALL OTHER CAUSES OF DEATH NOT COVERED IN THE PRECEDING CATEGORIES

accidental and violent deaths the male specific mortality curve lies far above the female, from youth until old age has set in about age 75. From that point on to the end of the span of life both curves ascend rapidly together, as a result of the deaths recorded as resulting from senility. Eventually it is to be expected that no deaths will be registered as resulting from senility. We shall have them all put more nearly where they belong.

These diagrams of specific forces of mortality give altogether a remarkably clear and definite picture of how death occurs among men. We see that failure of certain organ systems, such as the lungs, the heart, the kidneys, to maintain their structural and functional integrity, has an overwhelmingly great effect in determining the total rate of mortality as compared with some of the other organ systems. One can not but be impressed too with the essential orderliness of the phenomena we have examined. The probability of any particular organ system breaking down and causing death is mathematically definite at each age, and changes in a strikingly orderly manner as age changes, as is shown in Table 1. Thus we find that in the first year of life it is the alimentary tract and its associated organs which most frequently break down and cause death. From age 1 to age 60 the specific force of mortality from breakdown of the respiratory system is higher (with a few insignificant exceptions in the females) usually by a considerable amount, than that associated with any other organ system of the body. From 60 to 90 years of age the circulatory system takes the front rank, with a higher specific mortality rate than any other organ system.

TABLE I.

The Most Fatal Organ Systems at Different Ages

MALES			FEMALES	
Per cent of all biologically classifiable deaths due to breakdown of specified organ system.	Most fatal organ system	Age Group	Most fatal organ system	Per cent of all biologically classifiable deaths due to breakdown of specified organ system.
68.8	Alimentary tract	0 — 1	Alimentary tract	40.6
50.1	Respiratory	1 — 4	Respiratory	51.3
41.2	"	5 — 9	"	42.5
27.1	"	10—14	"	33.3
43.6	"	15—19	"	43.8
52.6	"	20—24	"	46.0
49.7	"	25—29	"	44.2
45.6	"	30—34	"	39.5
39.9	"	35—39	"	33.2
33.3	"	40—44	"	27.5
28.0	"	45—49	"	22.1
23.6	"	50—54	Alimentary tract	21.6
25.0	Circulatory	55—59	"	22.6
28.4	"	60—64	Circulatory	24.4
30.9	"	65—69	"	25.6
32.5	"	70—74	"	28.0
32.9	"	75—79	"	28.4
33.3	"	80—84	"	30.4
		85—89	"	30.8

If our lungs were as organically good relatively as our hearts, having regard in each case for the work the organ is called upon to do and the conditions under which it must do it, we should live a considerable number of years longer on the average than we do now. One can not but feel that the working out of a rational and scientifically grounded system of personal hygiene of the respiratory organs, on the broadest basis, to include all such matters as ventilation of buildings, etc., and the putting of such a personal hygiene into general use through education, would pay about as large dividends as could be hoped for from any investment in public health securities. I am aware that much has already been done in this direction, but in order to reap any such dividends as I am thinking of, a vast amount must be added to our present knowledge of the physiology, pathology, epidemiology, and every other aspect of the functions and structures of respiration.

4. The Embryological Basis of Mortality

Up to this point in our discussion we have confined our attention to the organological incidence of death. It is possible to push the matter of human mortality still farther back. In the embryological development of the vertebrate body, there are laid down at an early stage, in fact immediately following the process of gastrulation, three morphologically definite primitive tissue elements, called respectively the ectoderm, the mesoderm, and the endoderm. These are termed the

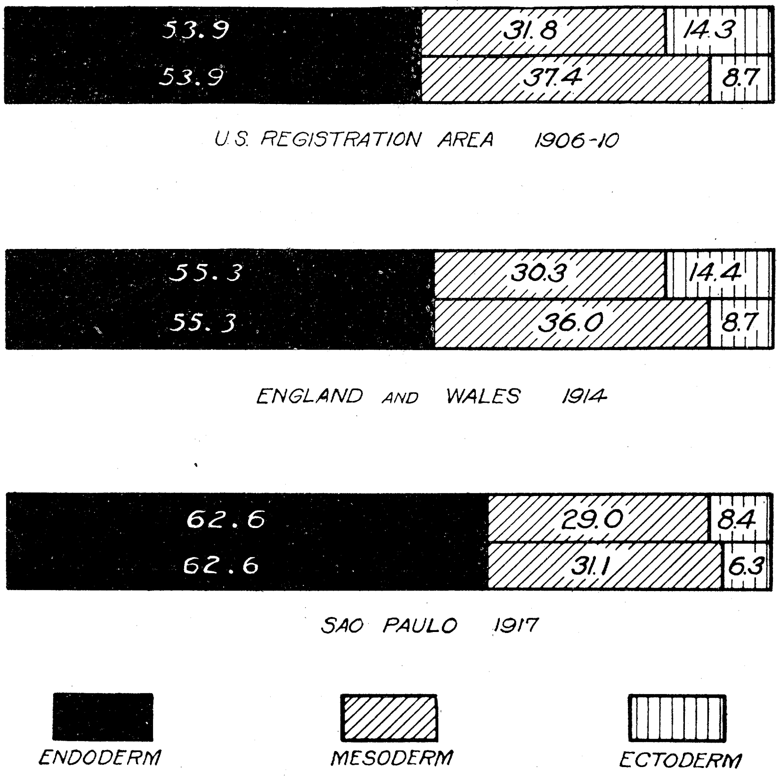

FIG. 13. DIAGRAM SHOWING THE PERCENTAGES OF BIOLOGICALLY CLASSIFIABLE HUMAN MORTALITY RESULTING FROM BREAKDOWN OF ORGANS DEVELOPING FROM THE DIFFERENT GERM LAYERS. Upper bar of pair gives upper limit of mortality chargeable to ectoderm: lower bar gives lower limit of mortality chargeable to ectoderm

germ-layers, and embryological science has, for a great many forms, succeeded in a broad way in tracing back to the primitive germ layer from which it originally started its development, substantially every one of the adult organs and organ systems of the body. It makes no difference to the validity or significance of the discussion which we are about to enter upon, in what degree of esteem or contempt in biological philosophy the germ layer theory or doctrine, which occupied so large a place in morphological speculation 50 years ago, may be held. We are here concerned only with the well established broad fact, that in general all adult organ systems may be traced back over the path of their embryological development to the germ layer, or combination of germ layers, from which they originally started.

Having arranged so far as possible all causes of death on an organological basis, it occurred to one to go one step further back and combine them under the headings of the primary germ layers from which the several organs developed embryologically. To do this was a task of considerable difficulty. It raised intricate, and in some cases still unsettled, questions of embryology. Furthermore, the original statistical rubrics under which the data are compiled by registrars of vital statistics were never planned with such an object as this in mind. Still the thing seemed worth trying because of the biological interest which would attach to the result, even though it were somewhat crude and in respect of minor and insignificant details open to criticism. It is not possible here to go into details as to how the causes of death were combined in making up the final tables. For these details one must refer to the original papers.

Fig. 13 gives the result for the crude mortality of the U. S. Registration Area, England and Wales, and Sao Paulo, Brazil. The figures show that in man, the highest product of organic evolution, about 57 per cent of all the biologically classifiable deaths result from a breakdown and failure further to function of organs arising from the endoderm in their embryological development, while but from 8 per cent to 13 per cent can be regarded as a result of breakdown of organ systems arising from the ectoderm. The remaining 30 to 35 per cent of the mortality results from failure of mesodermic organs. The two values stated for ectoderm and mesoderm, shown by the two bars in the diagram, differ by virtue of the fact that two important causes of death, cerebral hemorrhage and apoplexy, and softening of the brain, are put in the one case with the ectoderm and in the other case with the mesoderm. The pathological arguments for the one disposition as against the other of these two diseases are interesting, but lack of space prevents their exposition here. I have chosen rather to present the facts in both ways.

Taking a general view of comparative anatomy and embryology it is evident that in the evolutionary history through which man and the higher vertebrates have passed it is the ectoderm which has been most widely differentiated from its primitive condition, to the validity of which statement the central nervous system furnishes the most potent evidence. The endoderm has been least differentiated in the process of evolution, while the mesoderm occupies an intermediate position in this respect.

Degree of differentiation of organs in evolution implies degree of adaptation to environment. From the present point of view we see that that germ layer, the endoderm, which has evolved or become differentiated least in the process of evolution is least able to meet successfully the vicissitudes of the environment. The ectoderm has changed most in the course of evolution. Of this the central nervous system of man is the best proof. There have also been formed in the process of differentiation, protective mechanisms, the skull and vertebral column, which very well keep the delicate and highly organized central nervous system away from direct contact with the environment. The skin also exhibits many differentiations of a highly adaptive nature to resist environmental difficulties. It is then not surprising that the organ systems developed from the ectoderm break down and lead to death less frequently than any other. The figures make it clear that man's greatest enemy is his own endoderm. Evolutionally speaking, it is a very old-fashioned and out-of-date ancestral relic, which causes him an infinity of trouble. Practically all public health activities are directed towards overcoming the difficulties which arise because man carries about this antediluvian sort of endoderm. We endeavor to modify the environment, and soften its asperities down to the point where our own inefficient endodermal mechanism can cope with them, by such methods as preventing bacterial contamination of water, food and the like, warming the air we breathe, etc. But our ectoderm requires no such extensive amelioration of the environment. There are at most only a very few if any germs which can gain entrance to the body through the normal, healthy, unbroken skin. We do, to be sure, wear clothes. But it is at least a debatable question whether upon many parts of the earth's surface we should not be better off without them from the point of view of health.

These data indicate further in another manner how important are the fundamental embryological factors in determining the mortality of man. Of the three localities compared, England and the United States may be fairly regarded as much more advanced in matters of public health and sanitation than Sao Paulo. This fact is reflected with perfect precision and justice in the relative proportion of the death rates from endoderm and ectoderm. In the United States and England about 55 per cent. of the classifiable deaths are chargeable

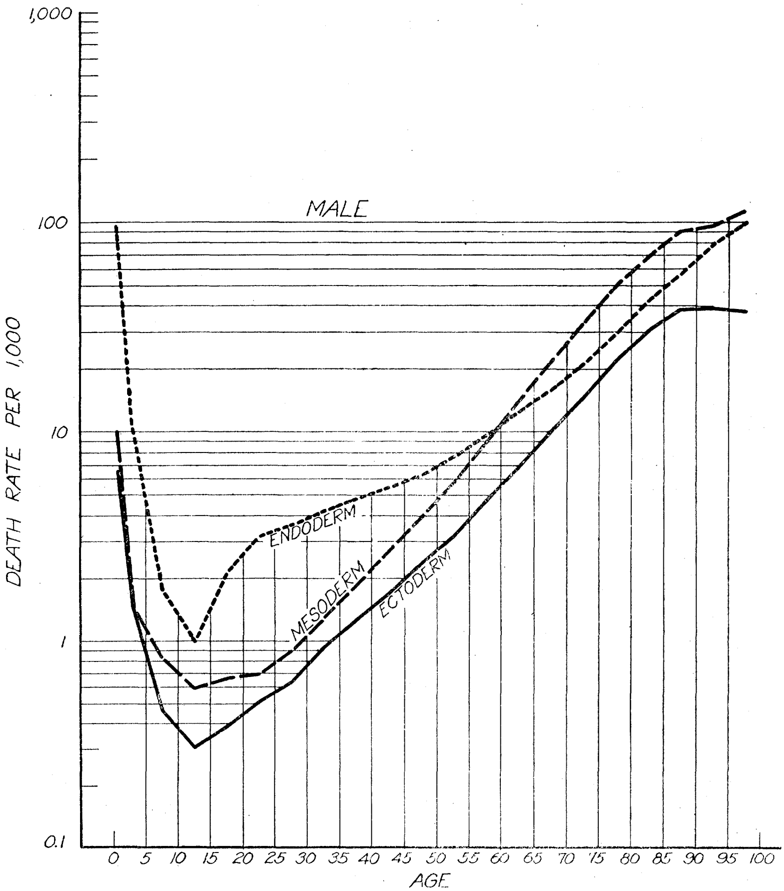

FIG. 14. SHOWING SPECIFIC DEATH RATES IN MALES ACCORDING TO THE GERM LAYER FROM WHICH THE ORGANS DEVELOPED WHERE BREAKDOWN LEADS TO DEATH

to endoderm and about 9 to 14.5 per cent to ectoderm. In Sao Paulo 62.6 per cent. fall with the endoderm, and but 6.3 to 8.4 per cent. with the ectoderm. Since, as we have already shown, public health measures can and do affect practically only the death rate chargeable to endoderm this result which is actually obtained is precisely that which would be expected.

A question which naturally occurs is as to what the age distribution of breakdown of ectodermic, mesodermic, or endodermic organs may be. Are the endodermic organs for example relatively more liable to breakdown in early life, and less so later, as general observation would lead one to conclude?

To answer this and similar questions which come to mind we need to distribute our specific rates upon an embryological basis.

In Fig. 14 the result of doing this is shown for males. We note that prior to age 60 the curve for the breakdown of organs of endo-

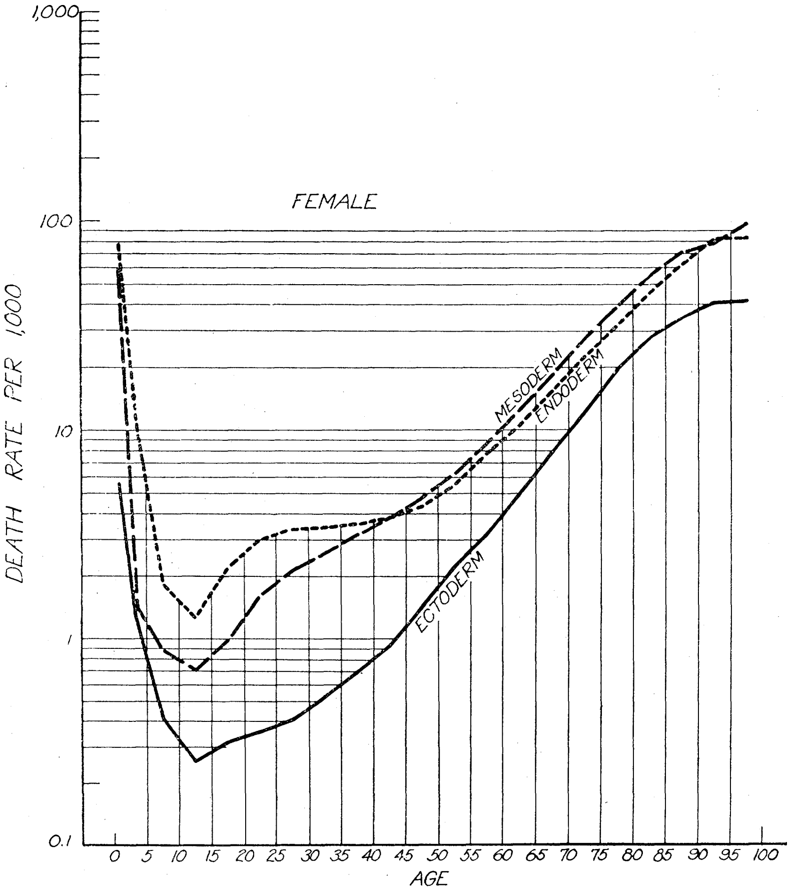

FIG. 15. SHOWING SPECIFIC DEATH RATES FOR FEMALES, CLASSIFIED IN THE SAME MANNER AS IN FIG. 14

dermic origin lies at the top of the diagram; next below it comes the curve for the breakdown of organs of mesodermic origin; and finally at the bottom the curve for the breakdown of organs of ectodermic origin. All three of the curves have in general the form of a specific death rate curve. The rates for all three germ layers are relatively high in infancy and drop at a practically constant rate to a low point in early youth. In infancy the heaviest mortality in males is due to the breakdown of organs of endodermic origin. This part of the death rate accounts for something like 10 times as many deaths as either mesoderm or ectoderm at this period of life. From about age 12 on in the case of organs of ectodermic origin, and from about age 22 on in cases of mesodermic origin, the death rate curves rise at a practically constant rate to extreme old age. The ectodermic and mesodermic curves during this portion of the life span are nearly parallel, diverging only slightly from each other with advancing age.

The curve for the death rate resulting from breakdown of organs of endodermic origin has an entirely different course. It rises sharply for ten years after the low point in early youth, and then makes a rather sharp bend at about age 22, and passes off to the end of the life span, at a reduced rate of change. In consequence of this it crosses the mesodermic line at age 60. From that point on to the end of life deaths from breakdown of organs of mesodermic origin stand first in importance.

Fig. 15 shows the same set of facts for the female, and at once a number of striking differences between the conditions in the two sexes appear. In the first place, the breakdown of mesodermic organs is practically of equal importance in determining the mortality of infants with the breakdown of endodermic organs, in the case of the female. This fact, of course, arises because of the heavy mortality of infancy due to failure of the female reproductive organs, a matter which has already been discussed. The curve for breakdown of the ectodermic organs follows substantially the same kind of course in the female as it does in the male. The mesoderm and endoderm lines cross nearly 20 years earlier in the case of females than in the males. This circumstance arises from the fact that throughout life the mesodermic organs play a relatively more important rôle in the determination of mortality in the female than they do in the male.

What reward in the way of useful generalizations may be claimed from the details reviewed? I hope that these facts will have served in some measure to complete and round out in clearer outlines one part of the picture of the general biology of death. It has been shown in what has preceded that natural death is not a necessary or inherent attribute or consequence of life. Many cells are potentially immortal and the potentiality is actually realized if appropriate conditions are provided. Protozoa are immortal. Germ cells are immortal. Various somatic cells, and even tissues have been proved to be potentially immortal by demonstrating in a variety of ways that under appropriate conditions they continue to live indefinitely. This is the lesson taught us on the one hand by successive transplantations of tumor cells, which are only modified somatic cells, and on the other hand by successful culture of many sorts of somatic cells *in vitro.*

Analytical consideration of the matter shows very clearly that why the somata of multicellular organisms die is because of the differentiations and specializations of structure and function which they exhibit in their make-up. Certain cells are differentiated to carry on certain specialized functions. In this specialization they forego their power of independent and indefinitely continued existence. The cells lining the lungs, for example, must depend in the body upon the unfailing normal activity of the cells of the alimentary tract and the blood in order that they, the epithelial cells of the lungs, may get proper nutrition. If in such an interlocking and mutually dependent system any one part through accident or in any way whatever gets deviated from its normal functioning, the balance of the whole system is upset. If the departure of any part from its normal functional course is great enough to be beyond correction promptly through the normal regulatory powers of the organism, death of the whole will surely ensue.

What I have tried to show in the present paper is a quantitative picture of how the different organ systems get out of balance, and wreck the whole machine. The broad orderliness and lawfulness of the whole business of human mortality is impressive. We have seen that different organ systems have well-defined times of breakdown. Or, put in another way, we see that in the human organism, just as in the automobile, the serviceability of the different parts varies greatly. The heart outwears the lungs, the brain outwears both. But we have further, I believe, got an inkling of the fundamental reason why these things are so. It is broadly speaking, because evolution is a purely mechanistic process instead of being an intelligent one. All the parts are not perfected by evolution to even an approximately equal degree. It is conceivable that an omnipotent person could have made a much better machine, as a whole, than the human body which evolution has produced. He would presumably have made an endoderm with as good resisting and wearing qualities as the mesoderm or ectoderm. Evolution by the haphazard process of trial and error which we call natural selection, makes each part only just good enough to get by. In the very nature of the process itself it can not possibly do anything any more constructive than this. The workmanship of evolution, from a mechanical point of view, is extraordinarily like that of the average automobile repair man. If evolution happens to be furnished by variation with fine materials, as in the case of the nervous system, it has no objection to using them, but it is equally ready to use the shoddiest of endoderm provided it will hold together just long enough to get the machine by the reproductive period.

It furthermore seems to me that the results presented in this paper add one more link to the already strong chain of evidence which indicates the highly important part played by innate constitutional biological factors as contrasted with environmental factors in the determination of the observed rates of human mortality. Here we have grouped human mortality into broad classes which rest upon a strictly biological basis. When this is done it is found that the proportionate subdivision of the mortality is strikingly similar in such widely dissimilar environments as the United States, England and Southern Brazil. It is inconceivable that such congruent results would appear if the environment were the predominant factor in human mortality.